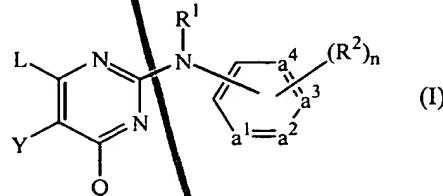


*C1*  
*TO4FO1*

8. (Twice Amended) A method of treating subjects suffering from HIV (Human Immunodeficiency Virus) infection comprising administering to the subject a therapeutically effective amount of a compound of formula



a *N*-oxide, a pharmaceutically acceptable addition salt, or a stereochemically isomeric form thereof, wherein

$-a^1=a^2-a^3=a^4-$  represents a bivalent radical of formula

- $-CH=CH-CH=CH-$  (a-1);
- $-N=CH-CH=CH-$  (a-2);
- $-N=CH-N=CH-$  (a-3);
- $-N=CH-CH=N-$  (a-4);
- $-N=N-CH=CH-$  (a-5);

$n$  is 0, 1, 2, 3 or 4; and in case  $-a^1=a^2-a^3=a^4-$  is (a-1), then  $n$  may also be 5;

$R^1$  is hydrogen; aryl; formyl;  $C_{1-6}$ alkylcarbonyl;  $C_{1-6}$ alkyl;  $C_{1-6}$ alkyloxycarbonyl;  $C_{1-6}$ alkyl substituted with formyl,  $C_{1-6}$ alkylcarbonyl,  $C_{1-6}$ alkyloxycarbonyl,  $C_{1-6}$ alkylcarbonyloxy;  $C_{1-6}$ alkyloxy $C_{1-6}$ alkylcarbonyl substituted with  $C_{1-6}$ alkyloxycarbonyl;

each  $R^2$  independently is hydroxy, halo,  $C_{1-6}$ alkyl optionally substituted with cyano or  $-C(=O)R^6$ ,  $C_{3-7}$ cycloalkyl,  $C_{2-6}$ alkenyl optionally substituted with one or more halogen atoms or cyano,  $C_{2-6}$ alkynyl optionally substituted with one or more halogen atoms or cyano,  $C_{1-6}$ alkyloxy,  $C_{1-6}$ alkyloxycarbonyl, carboxyl, cyano, nitro, amino, mono- or di( $C_{1-6}$ alkyl)amino, polyhalomethyl, polyhalomethoxy, polyhalomethylthio,  $-S(=O)_pR^6$ ,  $-NH-S(=O)_pR^6$ ,  $-C(=O)R^6$ ,  $-NHC(=O)H$ ,  $-C(=O)NHNH_2$ ,  $-NHC(=O)R^6$ ,  $-C(=NH)R^6$  or a radical of formula



*TO4D1*  
wherein each A independently is N, CH or  $CR^6$ ;

B is NH, O, S or  $NR^6$ ;

$p$  is 1 or 2; and

~~R<sup>6</sup> is methyl, amino, mono- or dimethylamino or polyhalomethyl;~~

~~L is C<sub>1-10</sub>alkyl, C<sub>2-10</sub>alkenyl, C<sub>2-10</sub>alkynyl, C<sub>3-7</sub>cycloalkyl, whereby each of said aliphatic group may be substituted with one or two substituents independently selected from~~

~~\* C<sub>3-7</sub>cycloalkyl,~~

~~\* indolyl or isoindolyl, each optionally substituted with one, two, three or four substituents each independently selected from halo, C<sub>1-6</sub>alkyl, hydroxy, C<sub>1-6</sub>alkyloxy, cyano, aminocarbonyl, nitro, amino, polyhalomethyl, polyhalomethoxy and C<sub>1-6</sub>alkylcarbonyl,~~

~~\* phenyl, pyridinyl, pyrimidinyl, pyrazinyl or pyridazinyl, wherein each of said aromatic rings may optionally be substituted with one, two, three, four or five substituents each independently selected from the substituents defined in R<sup>2</sup>; or~~

~~L is -X-R<sup>3</sup> wherein~~

~~R<sup>3</sup> is phenyl, pyridinyl, pyrimidinyl, pyrazinyl or pyridazinyl, wherein each of said aromatic rings may optionally be substituted with one, two, three, four or five substituents each independently selected from the substituents defined in R<sup>2</sup>; and~~

~~X is -NR<sup>1</sup>-, -NH-NH-, -N=N-, -O-, -C(=O)-, -CHOH-, -S-, -S(=O)- or -S(=O)<sub>2</sub>-;~~

~~Q represents hydrogen, C<sub>1-6</sub>alkyl, halo, polyhaloC<sub>1-6</sub>alkyl or -NR<sup>4</sup>R<sup>5</sup>; and~~

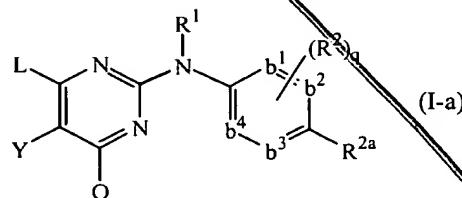
~~R<sup>4</sup> and R<sup>5</sup> are each independently selected from hydrogen, hydroxy, C<sub>1-12</sub>alkyl, C<sub>1-12</sub>alkyloxy, C<sub>1-12</sub>alkylcarbonyl, C<sub>1-12</sub>alkyloxycarbonyl, aryl, amino, mono- or di(C<sub>1-12</sub>alkyl)amino, mono- or di(C<sub>1-12</sub>alkyl)aminocarbonyl wherein each of the aforementioned C<sub>1-12</sub>alkyl groups may optionally and each individually be substituted with one or two substituents each independently selected from hydroxy, C<sub>1-6</sub>alkyloxy, hydroxyC<sub>1-6</sub>alkyloxy, carboxyl, C<sub>1-6</sub>alkyloxycarbonyl, cyano, amino, imino, mono- or di(C<sub>1-6</sub>alkyl)amino, polyhalomethyl, polyhalomethoxy, polyhalomethylthio, -S(=O)<sub>p</sub>R<sup>6</sup>, -NH-S(=O)<sub>p</sub>R<sup>6</sup>, -C(=O)R<sup>6</sup>, -NHC(=O)H, -C(=O)NHNH<sub>2</sub>, -NHC(=O)R<sup>6</sup>, -C(=NH)R<sup>6</sup>, aryl and Het; or~~

*C /  
1 /  
cont*

$R^4$  and  $R^5$  taken together may form pyrrolidinyl, piperidinyl, morpholinyl, or mono- or di( $C_{1-12}$ alkyl)amino $C_{1-4}$ alkylidene;  $Y$  represents hydroxy, halo,  $C_{3-7}$ cycloalkyl,  $C_{2-6}$ alkenyl optionally substituted with one or more halogen atoms,  $C_{2-6}$ alkynyl optionally substituted with one or more halogen atoms,  $C_{1-6}$ alkyl substituted with cyano or  $-C(=O)R^6$ ,  $C_{1-6}$ alkyloxy,  $C_{1-6}$ alkyloxycarbonyl, carboxyl, cyano, nitro, amino, mono- or di( $C_{1-6}$ alkyl)amino, polyhalomethyl, polyhalomethoxy, polyhalomethylthio,  $-S(=O)_pR^6$ ,  $-NH-S(=O)_pR^6$ ,  $-C(=O)R^6$ ,  $-NHC(=O)H$ ,  $-C(=O)NHNH_2$ ,  $-NHC(=O)R^6$ ,  $-C(=NH)R^6$  or aryl; aryl is phenyl or phenyl substituted with one, two, three, four or five substituents each independently selected from halo,  $C_{1-6}$ alkyl,  $C_{3-7}$ cycloalkyl,  $C_{1-6}$ alkyloxy, cyano, nitro, polyhalo $C_{1-6}$ alkyl and polyhalo $C_{1-6}$ alkyloxy; Het is an aliphatic or aromatic heterocyclic radical; said aliphatic heterocyclic radical is selected from pyrrolidinyl, piperidinyl, homopiperidinyl, piperazinyl, morpholinyl, tetrahydrofuranyl and tetrahydrothienyl wherein each of said aliphatic heterocyclic radical may optionally be substituted with an oxo group; and said aromatic heterocyclic radical is selected from pyrrolyl, furanyl, thienyl, pyridinyl, pyrimidinyl, pyrazinyl and pyridazinyl wherein each of said aromatic heterocyclic radical may optionally be substituted with hydroxy.

*C 2  
C 3  
TO 440*

219. (Once Amended) A method of treating non-nucleoside reverse transcriptase inhibitor resistant HIV infection in a subject in need thereof comprising administering to the subject an effective amount of a compound having the formula



a  $N$ -oxide, an addition salt, or a stereochemically isomeric form thereof, wherein

$-b^1=b^2-C(R^{2a})=b^3-b^4=$  represents a bivalent radical of formula

*C2*  
*C3*  
*cont*

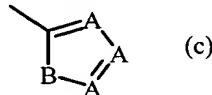
~~-CH=CH-C(R<sup>2a</sup>)=CH-CH= (b-1) ;~~  
~~-N=CH-C(R<sup>2a</sup>)=CH-CH= (b-2) ;~~  
~~-CH=N-C(R<sup>2a</sup>)=CH-CH= (b-3) ;~~  
~~-N=CH-C(R<sup>2a</sup>)=N-CH= (b-4) ;~~  
~~-N=CH-C(R<sup>2a</sup>)=CH-N= (b-5) ;~~  
~~-CH=N-C(R<sup>2a</sup>)=N-CH= (b-6) ;~~  
~~-N=N-C(R<sup>2a</sup>)=CH-CH= (b-7) ;~~

*q* is 0, 1, 2; or where possible *q* is 3 or 4;

*R<sup>1</sup>* is hydrogen; aryl; formyl; C<sub>1-6</sub>alkylcarbonyl; C<sub>1-6</sub>alkyl; C<sub>1-6</sub>alkyloxycarbonyl; C<sub>1-6</sub>alkyl substituted with formyl, C<sub>1-6</sub>alkylcarbonyl, C<sub>1-6</sub>alkyloxycarbonyl, C<sub>1-6</sub>alkylcarbonyloxy; C<sub>1-6</sub>alkyloxyC<sub>1-6</sub>alkylcarbonyl substituted with C<sub>1-6</sub>alkyloxycarbonyl;

*R<sup>2a</sup>* is cyano, aminocarbonyl, mono- or dimethylaminocarbonyl, C<sub>1-6</sub>alkyl substituted with cyano, aminocarbonyl or mono- or dimethylaminocarbonyl, C<sub>2-6</sub>alkenyl substituted with cyano, or C<sub>2-6</sub>alkynyl substituted with cyano;

each *R<sup>2</sup>* independently is hydroxy, halo, C<sub>1-6</sub>alkyl optionally substituted with cyano or -C(=O)R<sup>6</sup>, C<sub>3-7</sub>cycloalkyl, C<sub>2-6</sub>alkenyl optionally substituted with one or more halogen atoms or cyano, C<sub>2-6</sub>alkynyl optionally substituted with one or more halogen atoms or cyano, C<sub>1-6</sub>alkyloxy, C<sub>1-6</sub>alkyloxycarbonyl, carboxyl, cyano, nitro, amino, mono- or di(C<sub>1-6</sub>alkyl)amino, polyhalomethyl, polyhalomethyloxy, polyhalomethylthio, -S(=O)<sub>p</sub>R<sup>6</sup>, -NH-S(=O)<sub>p</sub>R<sup>6</sup>, -C(=O)R<sup>6</sup>, -NHC(=O)H, -C(=O)NNH<sub>2</sub>, -NHC(=O)R<sup>6</sup>, -C(=NH)R<sup>6</sup> or a radical of formula



wherein each A independently is N, CH or CR<sup>6</sup>;

B is NH, O, S or NR<sup>6</sup>;

*p* is 1 or 2; and

R<sup>6</sup> is methyl, amino, mono- or dimethylamino or polyhalomethyl;

*L* is C<sub>1-10</sub>alkyl, C<sub>2-10</sub>alkenyl, C<sub>2-10</sub>alkynyl, C<sub>3-7</sub>cycloalkyl, whereby each of said aliphatic group may be substituted with one or two substituents independently selected from

\* C<sub>3-7</sub>cycloalkyl,

\* indolyl or isoindolyl, each optionally substituted with one, two, three or four substituents each independently selected from halo, C<sub>1-6</sub>alkyl, hydroxy, C<sub>1-6</sub>alkyloxy, cyano, aminocarbonyl, nitro, amino, polyhalomethyl, polyhalomethyloxy and C<sub>1-6</sub>alkylcarbonyl,

\* phenyl, pyridinyl, pyrimidinyl, pyrazinyl or pyridazinyl, wherein each of said aromatic rings may optionally be substituted with one, two, three, four or five substituents each independently selected from the substituents defined in R<sup>2</sup>; or

*C 2*  
*C 3*  
*cont*

L is -X-R<sup>3</sup> wherein

R<sup>3</sup> is phenyl, pyridinyl, pyrimidinyl, pyrazinyl or pyridazinyl, wherein each of said aromatic rings may optionally be substituted with one, two, three, four or five substituents each independently selected from the substituents defined in R<sup>2</sup>; and

X is -NR<sup>1</sup>-, -NH-NH-, -N=N-, -O-, -C(=O)-, -CHOH-, -S-, -S(=O)- or -S(=O)<sub>2</sub>-;

Q represents hydrogen, C<sub>1-6</sub>alkyl, halo, polyhaloC<sub>1-6</sub>alkyl or -NR<sup>4</sup>R<sup>5</sup>; and

R<sup>4</sup> and R<sup>5</sup> are each independently selected from hydrogen, hydroxy, C<sub>1-12</sub>alkyl, C<sub>1-12</sub>alkyloxy, C<sub>1-12</sub>alkylcarbonyl, C<sub>1-12</sub>alkyloxycarbonyl, aryl, amino, mono- or di(C<sub>1-12</sub>alkyl)amino, mono- or di(C<sub>1-12</sub>alkyl)aminocarbonyl wherein each of the aforementioned C<sub>1-12</sub>alkyl groups may optionally and each individually be substituted with one or two substituents each independently selected from hydroxy, C<sub>1-6</sub>alkyloxy, hydroxyC<sub>1-6</sub>alkyloxy, carboxyl, C<sub>1-6</sub>alkyloxycarbonyl, cyano, amino, imino, mono- or di(C<sub>1-6</sub>alkyl)amino, polyhalomethyl, polyhalomethyloxy, polyhalomethylthio, -S(=O)<sub>p</sub>R<sup>6</sup>, -NH-S(=O)<sub>p</sub>R<sup>6</sup>, -C(=O)R<sup>6</sup>, -NHC(=O)H, -C(=O)NNH<sub>2</sub>, -NHC(=O)R<sup>6</sup>, -C(=NH)R<sup>6</sup>, aryl and Het; or

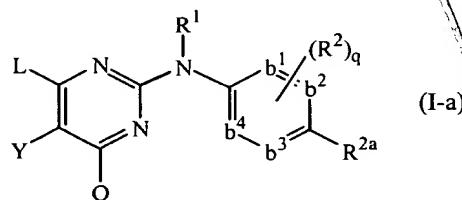
R<sup>4</sup> and R<sup>5</sup> taken together may form pyrrolidinyl, piperidinyl, morpholinyl, or mono- or di(C<sub>1-12</sub>alkyl)aminoC<sub>1-4</sub>alkylidene;

Y represents hydroxy, halo, C<sub>3-7</sub>cycloalkyl, C<sub>2-6</sub>alkenyl optionally substituted with one or more halogen atoms, C<sub>2-6</sub>alkynyl optionally substituted with one or more halogen atoms, C<sub>1-6</sub>alkyl substituted with cyano or -C(=O)R<sup>6</sup>,

~~C<sub>1-6</sub>alkyloxy, C<sub>1-6</sub>alkyloxycarbonyl, carboxyl, cyano, nitro, amino, mono- or di(C<sub>1-6</sub>alkyl)amino, polyhalomethyl, polyhalomethyloxy, polyhalomethylthio, -S(=O)<sub>p</sub>R<sup>6</sup>, -NH-S(=O)<sub>p</sub>R<sup>6</sup>, -C(=O)R<sup>6</sup>, -NHC(=O)H, -C(=O)NHNH<sub>2</sub>, -NHC(=O)R<sup>6</sup>, -C(=NH)R<sup>6</sup> or aryl;~~

aryl is phenyl or phenyl substituted with one, two, three, four or five substituents each independently selected from halo, C<sub>1-6</sub>alkyl, C<sub>3-7</sub>cycloalkyl, C<sub>1-6</sub>alkyloxy, cyano, nitro, polyhaloC<sub>1-6</sub>alkyl and polyhaloC<sub>1-6</sub>alkyloxy; Het is an aliphatic or aromatic heterocyclic radical; said aliphatic heterocyclic radical is selected from pyrrolidinyl, piperidinyl, homopiperidinyl, piperazinyl, morpholinyl, tetrahydrofuranyl and tetrahydrothienyl wherein each of said aliphatic heterocyclic radical may optionally be substituted with an oxo group; and said aromatic heterocyclic radical is selected from pyrrolyl, furanyl, thienyl, pyridinyl, pyrimidinyl, pyrazinyl and pyridazinyl wherein each of said aromatic heterocyclic radical may optionally be substituted with hydroxy.

3  
20. (Once Amended) A method of treating non-nucleoside reverse transcriptase inhibitor resistant HIV-1 infection in a subject in need thereof comprising administering to the subject an effective amount of a compound having the formula



a *N*-oxide, an addition salt, or a stereochemically isomeric form thereof, wherein

$-b^1 = b^2 - C(R^{2a}) = b^3 - b^4 =$  represents a bivalent radical of formula  
 $-CH=CH-C(R^{2a}) = CH-CH = (b-1);$   
 $-N=CH-C(R^{2a}) = CH-CH = (b-2);$   
 $-CH=N-C(R^{2a}) = CH-CH = (b-3);$   
 $-N=CH-C(R^{2a}) = N-CH = (b-4);$   
 $-N=CH-C(R^{2a}) = CH-N = (b-5);$

47

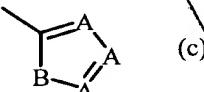
*13 cut*  
*C2*  
~~-CH=N-C(R<sup>2a</sup>)=N-CH= (b-6);~~

~~-N=N-C(R<sup>2a</sup>)=CH-CH= (b-7);~~

*q is 0, 1, 2; or where possible q is 3 or 4;*  
*R<sup>1</sup> is hydrogen; aryl; formyl; C<sub>1-6</sub>alkylcarbonyl; C<sub>1-6</sub>alkyl; C<sub>1-6</sub>alkyloxycarbonyl; C<sub>1-6</sub>alkyl substituted with formyl, C<sub>1-6</sub>alkylcarbonyl, C<sub>1-6</sub>alkyloxycarbonyl, C<sub>1-6</sub>alkylcarbonyloxy; C<sub>1-6</sub>alkyloxyC<sub>1-6</sub>alkylcarbonyl substituted with C<sub>1-6</sub>alkyloxycarbonyl;*

*R<sup>2a</sup> is cyano, aminocarbonyl, mono- or dimethylaminocarbonyl, C<sub>1-6</sub>alkyl substituted with cyano, aminocarbonyl or mono- or dimethylaminocarbonyl, C<sub>2-6</sub>alkenyl substituted with cyano, or C<sub>2-6</sub>alkynyl substituted with cyano;*

*each R<sup>2</sup> independently is hydroxy, halo, C<sub>1-6</sub>alkyl optionally substituted with cyano or -C(=O)R<sup>6</sup>, C<sub>3-7</sub>cycloalkyl, C<sub>2-6</sub>alkenyl optionally substituted with one or more halogen atoms or cyano, C<sub>2-6</sub>alkynyl optionally substituted with one or more halogen atoms or cyano, C<sub>1-6</sub>alkyloxy, C<sub>1-6</sub>alkyloxycarbonyl, carboxyl, cyano, nitro, amino, mono- or di(C<sub>1-6</sub>alkyl)amino, polyhalomethyl, polyhalomethyloxy, polyhalomethylthio, -S(=O)<sub>p</sub>R<sup>6</sup>, -NH-S(=O)<sub>p</sub>R<sup>6</sup>, -C(=O)R<sup>6</sup>, -NHC(=O)H, -C(=O)NNH<sub>2</sub>, -NHC(=O)R<sup>6</sup>, -C(=NH)R<sup>6</sup> or a radical of formula*



*wherein each A independently is N, CH or CR<sup>6</sup>;*

*B is NH, O, S or NR<sup>6</sup>;*

*p is 1 or 2; and*

*R<sup>6</sup> is methyl, amino, mono- or dimethylamino or polyhalomethyl;*

*L is C<sub>1-10</sub>alkyl, C<sub>2-10</sub>alkenyl, C<sub>2-10</sub>alkynyl, C<sub>3-7</sub>cycloalkyl, whereby each of said aliphatic group may be substituted with one or two substituents independently selected from*

*\* C<sub>3-7</sub>cycloalkyl,*

*\* indolyl or isoindolyl, each optionally substituted with one, two, three or four substituents each independently selected from halo, C<sub>1-6</sub>alkyl, hydroxy, C<sub>1-6</sub>alkyloxy, cyano, aminocarbonyl, nitro, amino, polyhalomethyl, polyhalomethyloxy and C<sub>1-6</sub>alkylcarbonyl,*

phenyl, pyridinyl, pyrimidinyl, pyrazinyl or pyridazinyl, wherein each of said aromatic rings may optionally be substituted with one, two, three, four or five substituents each independently selected from the substituents defined in R<sup>2</sup>; or

*C<sub>2</sub>*  
*C<sub>3</sub>*  
cont

L is -X-R<sup>3</sup> wherein

R<sup>3</sup> is phenyl, pyridinyl, pyrimidinyl, pyrazinyl or pyridazinyl, wherein each of said aromatic rings may optionally be substituted with one, two, three, four or five substituents each independently selected from the substituents defined in R<sup>2</sup>; and

X is -NR<sup>1</sup>-, -NH-NH-, -N=N-, -O-, -C(=O)-, -CHOH-, -S-, -S(=O)- or -S(=O)<sub>2</sub>-;

Q represents hydrogen, C<sub>1-6</sub>alkyl, halo, polyhaloC<sub>1-6</sub>alkyl or -NR<sup>4</sup>R<sup>5</sup>; and

R<sup>4</sup> and R<sup>5</sup> are each independently selected from hydrogen, hydroxy, C<sub>1-12</sub>alkyl, C<sub>1-12</sub>alkyloxy, C<sub>1-12</sub>alkylcarbonyl, C<sub>1-12</sub>alkyloxycarbonyl, aryl, amino, mono- or di(C<sub>1-12</sub>alkyl)amino, mono- or di(C<sub>1-12</sub>alkyl)aminocarbonyl wherein each of the aforementioned C<sub>1-12</sub>alkyl groups may optionally and each individually be substituted with one or two substituents each independently selected from hydroxy, C<sub>1-6</sub>alkyloxy, hydroxyC<sub>1-6</sub>alkyloxy, carboxyl, C<sub>1-6</sub>alkyloxycarbonyl, cyano, amino, imino, mono- or di(C<sub>1-6</sub>alkyl)amino, polyhalomethyl, polyhalomethyloxy, polyhalomethylthio, -S(=O)<sub>p</sub>R<sup>6</sup>, -NH-S(=O)<sub>p</sub>R<sup>6</sup>, -C(=O)R<sup>6</sup>, -NHC(=O)H, -C(=O)NNH<sub>2</sub>, -NHC(=O)R<sup>6</sup>, -C(=NH)R<sup>6</sup>, aryl and Het; or

R<sup>4</sup> and R<sup>5</sup> taken together may form pyrrolidinyl, piperidinyl, morpholinyl, or mono- or di(C<sub>1-12</sub>alkyl)aminoC<sub>1-4</sub>alkylidene;

Y represents hydroxy, halo, C<sub>3-7</sub>cycloalkyl, C<sub>2-6</sub>alkenyl optionally substituted with one or more halogen atoms, C<sub>2-6</sub>alkynyl optionally substituted with one or more halogen atoms, C<sub>1-6</sub>alkyl substituted with cyano or -C(=O)R<sup>6</sup>, C<sub>1-6</sub>alkyloxy, C<sub>1-6</sub>alkyloxycarbonyl, carboxyl, cyano, nitro, amino, mono- or di(C<sub>1-6</sub>alkyl)amino, polyhalomethyl, polyhalomethyloxy, polyhalomethylthio, -S(=O)<sub>p</sub>R<sup>6</sup>, -NH-S(=O)<sub>p</sub>R<sup>6</sup>, -C(=O)R<sup>6</sup>, -NHC(=O)H, -C(=O)NNH<sub>2</sub>, -NHC(=O)R<sup>6</sup>, -C(=NH)R<sup>6</sup> or aryl;

aryl is phenyl or phenyl substituted with one, two, three, four or five substituents each independently selected from halo, C<sub>1-6</sub>alkyl, C<sub>3-7</sub>cycloalkyl, C<sub>1-6</sub>alkyloxy, cyano, nitro, polyhaloC<sub>1-6</sub>alkyl and polyhaloC<sub>1-6</sub>alkyloxy; Het is an aliphatic or aromatic heterocyclic radical; said aliphatic heterocyclic radical is selected from pyrrolidinyl, piperidinyl, homopiperidinyl, piperazinyl, morpholinyl, tetrahydrofuranyl and tetrahydrothienyl wherein each of said aliphatic heterocyclic radical may optionally be substituted with an oxo group; and said aromatic heterocyclic radical is selected from pyrrolyl, furanyl, thienyl, pyridinyl, pyrimidinyl, pyrazinyl and pyridazinyl wherein each of said aromatic heterocyclic radical may optionally be substituted with hydroxy.